UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,464	04/29/2002	Peter L. Oren	29342/36230A	6930

4743 7590 03/03/2005

MARSHALL, GERSTEIN & BORUN LLP
6300 SEARS TOWER
233 S. WACKER DRIVE
CHICAGO, IL 60606

EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	
ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 03/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,464	OREN ET AL.	
	Examiner	Art Unit	
	Lakshmi S. Channavajjala	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,18-25 and 28-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,18-25 and 28-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of amendment and remarks dated 9-27-04 is acknowledged.

Claims 17 and 26-27 were canceled. New claims 28-36 have been added. Claims 1-16, 18-25 and 28-37 are pending.

In view of the amendment presented, the following new rejection is applied to the pending claims:

Newly presented composition claims are also included in he rejection for the reasons mentioned below:

Claim Rejections - 35 USC § 103

Claims 1-16, 18-25 and 28-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/03675 (Daung) in view of WO 96/38131 (Butler) and US 4,721,709 to Seth et al (Seth).

Daung teaches the claimed beta-carboline compounds and compositions containing the compounds, as also acknowledged by applicants on page 2 of the instant application. Daung specifically discloses teaches instant preferred compound (instant specification, page 3, lines 28-30) for treating conditions where inhibition of PDE5 is beneficial (see page 3, lines 24-25, lines 30-32 and is also referred to as compound A). On page 12, lines 11-12, Daung teaches that the compounds a and B are prepared as different dosage forms and in particular, Table B shows a tablet prepared by wet granulation, where in the tablet composition contains beta-carboline drug as active agent and other excipients such as polyvinylpyrrolidone, PEG, Polysorbate 80, magnesium stearate, crosscaramellose sodium, and microcrystalline cellulose, which

read on the instant claimed binder, diluent, wetting agent, lubricant and disintegrant respectively. Instant dependent claims specifically recite the excipients of Table B of Daung. With respect to the percentages of active ingredients and the excipients claimed, the total weight of the composition of tablet in Table B is 500 mg. A calculation of the proportion of each ingredient in Table 2 reads on the instant claimed percentages. With respect to the claimed "free drug", Daung does not teach an intimately embedded drug in a polymeric co-precipitate and hence meets the definition of instant "free drug" (instant page 5, lines 24-27). Instead, Daung only teaches direct compression or wet granulation followed by compression to prepare the tablets (pages 12-14).

Daung fails to teach the claimed particulates and sizes of particles, exact or the percentages of diluent (claim 5), lubricant (claim 8), binder (claim 10), and the claimed amounts of drug in tablet (claims 22, 23) and capsule (claim 25). However as acknowledged by applicants, Daung teaches the active agent and also for the same purposes i.e., as a 5PDE inhibitor. Further Daung teaches the same pharmaceutical compositions containing the same active compound and excipients, as claimed, in the form of tablets and capsules. Accordingly, optimizing the amounts of art recognized excipients such as binder, lubricant, optimizing the amount of active compound with an expectation to achieve the appropriate dosage form as well the desired therapeutic efficiency of the drug would have been within the scope of a skilled artisan because Daung suggests optimizing the amounts of drug in the range of 0.5 to 800 mg per day

and also employing the suitable excipients depending on the route of administration (page 5).

Butler teaches pharmaceutical compositions comprising beta-carboline compounds (abstract, page 4, lines 15-21). The specific beta-carboline compound taught by Butler is the same as that claimed in the instant invention. Further, Butler teaches that the above are poorly soluble in nature. Butler teaches solid dispersions but fails to teach the claimed particle sizes.

Seth teaches pharmaceutical composition containing poorly water-soluble drugs and a method of preparing the same. The method of Seth is practically applicable to all water insoluble drugs and comprises the steps of providing dry powder of the insoluble drug that is adsorbed on to a carrier such as starch or cellulose and is characterized in that the drug is present particulate form and at least 95% of the drug particles have a mean size of less than 15 microns (col. 4, lines 44-53, col. 3, lines 60-67), which is in the same range as claimed. Seth teaches that the drug particles are closely associated with the carrier and details the method of preparing the formulation in col. 6, lines 1-39. Further, Seth teaches preparation of various dosage forms such as tablets, capsules etc., with the above prepared formulation (col. 8). Examiner notes that instant specification refers to US patent 4,605,517 by incorporation for the preparation of the instant drug formulation. It is noted that the above patent also recites the same method of preparation as that of Seth. Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to prepare drug formulations of beta-carboline of Daung containing the excipients such as lubricants, wetting agents

etc., by the process of Seth i.e., particulate drug adsorbed on to excipients or carrier and compressing into tablets because Seth teaches that the conventional methods of jet milling or pin milling employed in drug preparation result in slow dissolution and absorption, (col. 2, lines 1-20) and that their method avoids the disadvantages of agglomeration and poor flow seen in the conventional methods. Accordingly, the expected result would be an increased dissolution of beta-carboline and hence increased bioavailability without agglomeration.

Double Patenting

Claims 1-16, 18-25 and 28-37 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 8, 9, 12-21 and 22-24 of copending Application No. 10/031,531and over claims 1-9 and14-16 of copending Application No. 10/031,463. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claimed composition containing a free drug, beta-carboline together with excipients and also composition comprising particulate form of the drug is also claimed in the above patent applications. US application 10/031,531 the composition of the instant claims in the form of capsules, which is reads on the claimed subject matter of instant claim 25. Further, method of treating specific disorders using the above composition by '131 anticipates instant method of treatment. Accordingly, claims of application 10/031,531 anticipate instant claims.

US application 10/031,463 claims a free drug particulate form of beta-carboline, compositions containing the free drug, a method of treating a patient in need thereof. The copending claims also recite particle sizes, carriers or excipients, which read on the instant dependent claims. Accordingly, the copending claims directed specifically to particulate beta-carboline compound, composition containing particulate compound anticipate instant broadly recited pharmaceutical compositions and method claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments filed 9-27-04 have been fully considered but they are not persuasive.

In response to applicants' amendment to instant claims, examiner has withdrawn the following rejections:

Rejection of claims 1-4, 6, 7, 9, 11-16 and 26 as being anticipated by WO (Daugan).

Rejection of claims 5, 8, 10, 19 and 22-25 as being obvious over Daugan. However, instant claims are now rejected as being obvious over Daung in view of Butler (WO '131) and Seth et al ('709) (see above).

Applicants argue that WO fails to teach the particle size of compound I in claim 1. It is argued that instant compounds are highly water-insoluble that are not easy to formulate into pharmaceutical formulations and that an intensive research resulted in

providing a stable composition of the instant compounds with improved dissolution and in vivo absorption. Applicants admits that WO '131 is directed to improving the bioavailability of poorly-soluble drugs, like compound I, but states that is achieved by co-precipitate dispersion and avoids a free form of poorly-water soluble drug. However, WO '131 nowhere compares and teaches away from preparing a free drug formulation as opposed to the preferred co-precipitate. Besides, instant specification states that instant formulation preferably contains a free drug form of the compound claimed, but fails to provide any unexpected results with the free drug form versus a co-precipitate form. The rejection clearly cites the teachings of WO '131 to show that the compounds claimed are known to be poorly soluble and not for the claimed particle sizes. Accordingly, the argument that the WO '131 fails to teach the particle sizes is moot.

Applicants argue that '709 fail to cure the deficiencies of the combined teachings of WO '675 and WO '131 because the patent merely teaches fine particle benzodiazepine drugs, which are different from the claimed compound. While it is true that instant claims do not recite a method of manufacturing adsorbed drug, as taught by '709 or US 4,605,517, the reference '709 teaches employing particulate material to improve dissolution and also avoid the problems of agglomeration and poor flow. Thus, the motivation to employ a particulate compound in the teachings of Daung comes from the teaching that the compounds are poorly soluble (WO '131) and that preparing fine particles of a poorly soluble drug improves the dissolution (Seth, '709).

Double patenting Rejection:

Applicants argue that patent disclosure may not be used as a prior art in determining if claims in any application are mere obvious variation of an invention. While applicants admit that instant application claims encompass a tablet, capsule or other solid formulation, applicants argue that the claims of 10/031,531 is a suspension formulation of a compound in a liquid. However, applicants' arguments are not persuasive because instant claims does not state the composition is solid and therefore the claimed formulation is generic to various dosage forms such as tablets, soft or hard capsules.

Applicants argue that the claims of application no. 10/031,463 merely recite the composition and not any specific carriers, diluents or excipients, as claimed in the instant. However, applicants' arguments are not persuasive because merely adding a suitable carrier or excipient to a known pharmaceutical composition is within the scope of a one of an ordinary skill in the art of preparing pharmaceutical formulations. Examiner notes that instant new claim 37 does not specify any carrier or diluent etc.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 9.00 AM -6.30 PM

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lakshmi S Channavajjala
Examiner
Art Unit 1615

February 26, 2005

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600